AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION:

Please replace the paragraphs beginning on page 10, line 20 and extending to page 12, line 17 with the following amended paragraphs:

--In sum, the present invention pertains to:

[1] a DNA encoding a polypeptide comprising an entire sequence of the amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, or a polypeptide comprising the polypeptide described above, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[2] a DNA encoding a polypeptide resulting from at least one of deletion, addition, insertion, or substitution of one or more amino acid residues in an entire sequence of the amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[3] a DNA comprising an entire sequence of the nucleotide sequence as shown by SEQ ID NO: 1 or a partial sequence thereof, or a DNA comprising the DNA described above, wherein any of the DNAs encodes a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[4] a DNA resulting from at least one of deletion, addition, insertion, or substitution of one or more bases in a DNA comprising an entire sequence of the nucleotide sequence as shown by SEQ ID NO: 1 or a partial sequence thereof, or a DNA comprising the DNA, wherein any of the DNAs encodes a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[5] a DNA being capable of hybridizing under stringent conditions with the DNA of any one of items [1] to [4] above, and encoding a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[6] a polypeptide encoded by the DNA of any one of items [1] to [5] above, wherein the polypeptide has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[7] a polypeptide comprising an entire amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, or a polypeptide comprising the polypeptide described above, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

[8] a polypeptide resulting from at least one of deletion, addition, insertion, or substitution of one or more amino acid residues in an entire amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, wherein the

polypeptide has an activity of a receptor capable of binding to a murine PBSF/SDF-1;--

Please replace the paragraphs beginning on page 19, line 18 and extending to page 20, line 24 with the following amended paragraphs:

--1) a DNA encoding a polypeptide comprising an entire sequence of the amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, or a polypeptide comprising the polypeptide described above, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

2) a DNA encoding a polypeptide resulting from at least one of deletion, addition, insertion, or substitution of one or more amino acid residues in an entire sequence of the amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF-1;

3) a DNA comprising an entire sequence of the nucleotide sequence as shown by SEQ ID NO: 1 or a partial sequence thereof, or a DNA comprising the DNA, wherein any of the DNAs encodes a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1;

4) a DNA resulting from at least one of deletion, addition, insertion, or substitution of one or more bases in a DNA comprising an entire sequence of the nucleotide sequence as shown by SEQ ID NO: 1 or a partial sequence thereof, or a DNA comprising the DNA, wherein any of the DNA encodes a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1; and

5) a DNA being capable of hybridizing under stringent conditions with the DNA of any one of items 1) to 4) above, and encoding a polypeptide having an activity of a receptor capable of binding to a murine PBSF/SDF-1.--

Please replace the paragraphs beginning on page 22, line 25 and extending to page 23, line 25 with the following amended paragraphs:

--The nucleotide sequence of a cDNA or the nucleotide sequence of a genomic DNA thus obtained is subjected to its nucleic acid homology search, referring to, for example, GenBank/EMBL/DDBJ DNA sequence data base, and whereby whether or not the cDNA obtained encodes a chemokine receptor can be deduced. SEQ ID NO: 1 shows the nucleotide sequence of the cDNA obtained. Since the nucleotide sequence spanning from 120-position to 1196-position in SEQ ID NO: 1 is the longest open reading frame, the amino acid sequence (SEQ ID NO: 2 ~~SEQ ID NO: 17~~) deduced on the basis of the

nucleotide sequence of this open reading frame is subjected to its homology search, using a program such as DNASIS (HITACHI, LTD.) or BLAST [Altschul, F. et al., *J. Mol. Biol.*, **215**, 403-410], to a database such as Genbank, EMBL or DDBJ, whereby the polypeptide encoded by the DNA of the present invention can be further studied.

As a result, the polypeptide having the amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ has been deduced to be a trimer G protein-coupled receptor covering a seven transmembrane-spanning domain, characteristic to a chemokine receptor. In addition, as a result of comparison with the amino acid sequences of known CXC chemokine receptors, there has been revealed that a human CXCR4/fusin/HUMSTSR is most closely resembles it (90% identity).--

Please replace the paragraphs beginning on page 28, line 5 with the following amended paragraphs:

--2. Polypeptide of the Present Invention

The polypeptide of the present invention includes, for instance, the following:

1) a polypeptide encoded by the DNA of the present invention, wherein the polypeptide has an activity of a receptor capable of binding to a murine PBSF/SDF;

2) a polypeptide comprising an entire amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, or a polypeptide comprising the polypeptide described above, wherein any of the polypeptides has an activity of a receptor capable of binding to a murine PBSF/SDF;

3) a polypeptide resulting from at least one of deletion, addition, insertion, or substitution of one or more amino acid residues in an entire amino acid sequence as shown by SEQ ID NO: 2 ~~SEQ ID NO: 17~~ or a partial sequence thereof, wherein the polypeptide has an activity of a receptor capable of binding to a murine PBSF/SDF; and

4) the polypeptide according to any one of items 1) to 3) above, derived from a murine pre-B-cell line DW34.--

Please replace the paragraphs beginning on page 41, line 20 and extending to page 42, line 4 with the following amended paragraphs:

--(1) Synthesis of Primer

Based on a known amino acid sequence of a chemokine receptor, a condensed forward primer C2F2-2 (SEQ ID NO: 9 ~~SEQ ID NO: 5~~) to a DNA sequence encoding an amino acid sequence of a second transmembrane-spanning domain, and a condensed reverse primer C4R1 (SEQ ID NO: 10 ~~SEQ ID NO: 6~~) to a DNA

sequence encoding an amino acid sequence of a seventh transmembrane-spanning domain were synthesized using a DNA synthesizer ("Cyclone Plus," Nippon Millipore).--

Please replace the paragraphs beginning on page 42, line 13 and extending to page 43, line 15 with the following amended paragraphs:

--(3)Cloning of cDNA Fragment of Murine CXCR4

A single-stranded cDNA was synthesized from 200 ng of mRNA purified from a murine pre-B-cell line DW34 with Ready-To-Go T-Primed First-Strand Kit (Pharmacia). PCR reaction (30 cycles under conditions of 94°C for 0.5 minutes, 55°C for 0.5 minutes, and 72°C for 1 minute) was carried out using the resulting single-stranded cDNA as a template, C2F2-2 and C4R1 as primers, and Taq as a thermostable DNA polymerase. The resulting reaction mixture was separated by low-melting point agarose gel electrophoresis, and a DNA band of a desired size (about 690 bp) was excised, and a DNA fragment was purified by using Wizard PCR Preps DNA Purification System (Promega). The resulting DNA fragment was inserted into pT7Blue vector by using a DNA Ligation Kit (Takara). The nucleotide sequence of the inserted DNA was determined by PRISM Ready Reaction Sequence Kit (Applied Biosystems) and DNA Sequencer (Applied Biosystems). The resulting cDNA sequence of a murine CXCR4 is shown by SEQ ID NO:

3 ~~SEQ ID NO: 2~~. Based on the cDNA sequence of a murine CXCR4 obtained in the manner described above, primers as shown by SEQ ID NO: 11 ~~SEQ ID NO: 7~~ and as shown by SEQ ID NO: 12 ~~SEQ ID NO: 8~~ were synthesized, and a cDNA clone containing 5'-terminal was obtained using the cDNA of DW34 cells obtained as described above as a template, with Marathon cDNA Amplification Kit (Clontech). The resulting cDNA sequence of a murine CXCR4 is shown by SEQ ID NO: 5 ~~SEQ ID NO: 3~~.--

Please replace the paragraphs beginning on page 43, line 19 and extending to page 44, line 15 with the following amended paragraphs:

--(1) Preparation of Probe

In order to study the expression of a murine CXCR4 in each murine tissue, firstly, a probe was prepared as follows. Based on the nucleotide sequence of a murine CXCR4 gene, a DNA sequence (SEQ ID NO: 19 ~~SEQ ID NO: 15~~) in the same direction corresponding to the second transmembrane-spanning-domain portion, and a DNA sequence (SEQ ID NO: 20 ~~SEQ ID NO: 16~~) in the opposite direction corresponding to the seventh transmembrane-spanning-domain portion were synthesized as primers to be used in the subsequent PCR. PCR reaction was carried out for 30 cycles under conditions of 94°C for 1 minute, 55°C for 1 minute, and 72°C for 2 minutes, using the cDNA of the nucleotide sequence obtained in Item (3) of

Example 1 above as a template, and a Taq Polymerase. The resulting reaction mixture of the PCR was separated by agarose gel electrophoresis, and a DNA band of a desired size (about 690 bp) was excised, and a DNA fragment was purified by using Wizard PCR Preps DNA Purification System. Fifty nanograms of the resulting DNA fragment was ^{32}P-labeled by using Prime-It II Random Primer Labelling Kit (Stratagene) to be used as a probe.--

Please replace the paragraph beginning on page 46, line 22 and extending to page 47, line 19 with the following amended paragraph:

--The cloned phage DNA was cleaved with various restriction enzymes, and separated by agarose gel electrophoresis. Those bands having the same patterns were considered to be the same clone, and the cloned phage DNA was cleaved such that a positive band of the size as small as possible could be obtained by repeating the same hybridization. The selected positive DNA fragment was inserted into a pBluescripts KSII vector, and the nucleotide sequence was determined by dideoxy method. The resulting DNA sequence of the murine CXCR4 gene is shown by SEQ ID NO: 7 ~~SEQ ID NO: 4~~. A nucleotide sequence containing the longest open reading frame was found from the nucleotide sequence as shown by SEQ ID NO: 5 ~~SEQ ID NO: 3~~ and the nucleotide sequence as shown by SEQ ID NO: 7 ~~SEQ ID NO: 4~~, and its nucleotide

sequence is shown by SEQ ID NO: 1. Also, this nucleotide sequence as shown by SEQ ID NO: 1 was subjected to nucleic acid homology search with the GenBank/EMBL/DDBJ DNA sequence data base. As a result of the search, it was clarified that the resulting clone is a DNA encoding a novel murine chemokine receptor, and the clone was named murine CXCR4.--

Please replace the paragraphs beginning on page 47, line 21 and extending to page 48, line 11 with the following amended paragraphs:

--Example 4 (Homology Analysis of Amino Acid Sequence of Murine CXCR4)

The amino acid sequence (SEQ ID NO: 2 ~~SEQ ID NO: 17~~) which was deduced based on the nucleotide sequence of a murine CXCR4 was estimated to be a trimer G protein-coupled receptor containing a seven transmembrane-spanning domain, characteristic to a chemokine receptor. The amino acid sequence thereof was compared with a known sequence of a CXC chemokine receptor (GenBank, EMBL, DDBJ were used as data base, and analyzed with BLAST). As a result, the analyzed sequence most closely resembled human CXCR4/fusin/HUMSTSR (90% identity), and homologies with monkey CXCR4 and bovine CXCR4 were 89% and 86%, respectively, and homologies with rat IL-8RB, rabbit IL-8RA, and rabbit IL-8RB were 49%, 47%, and 45%, respectively.--

Please replace the paragraphs beginning on page 48, line 16 and extending to page 50, line 11 with the following amended paragraphs:

--(1)Preparation for Expression Vectors of Murine CXCR4, Human CCCRR2B and Human CXCR4/fusin/HUMSTSR

In order to clone previously reported human chemokine receptors a CC CKR2B gene and a CXCR4/fusin/HUMSTSR gene, PCR reaction was carried out in the following manner using a cDNA of a human monocyte cell line THP-1. Five-hundred nanograms of a cDNA of the THP-1 cells was used as a template, the primers as shown by SEQ ID NO: 15 ~~SEQ ID NO: 11~~ and SEQ ID NO: 16 ~~SEQ ID NO: 12~~ were used for amplification of human CXCR4/fusin/HUMSTSR, and the primers as shown by SEQ ID NO: 13 ~~SEQ ID NO: 9~~ and SEQ ID NO: 14 ~~SEQ ID NO: 10~~ were used for amplification of CC CKR2B, each primer of which was used in an amount of 500 ng. As the enzyme for the reaction, Taq Polymerase (Takara Shuzo) was used. The reaction was carried out for 1 cycle at 94°C for 3 minutes; thereafter, 35 cycles at 94°C for 1 minute, 55°C for 2 minutes, and 72°C for 3 minutes; and further at 72°C for 3 minutes. The gene fragments of human CXCR4/fusin/HUMSTSR and CC CKR2B obtained by the reaction were each incorporated into TA cloning sites of pCRII (Invitrogen). The plasmids obtained in the manner described above were named

pCRIICXCR4 and pCRIICC CKR2B, respectively. Subsequently, the resulting pCRIICXCR4 and pCRIICC CKR2B plasmids were respectively digested with NotI and XboI (both from Takara Shuzo), and the digested fragment was incorporated into a NotI/XboI site of pCAGGStkNeo. The plasmids obtained in the manner described above were named pCANCXCR4 and pCANCC CKR2B, respectively.

In order to clone the murine CXCR4 gene, PCR technique was carried out using a single-stranded cDNA of the murine pre-B-cell line DW34 as shown by SEQ ID NO: 5 ~~SEQ ID NO: 3~~ obtained in Item (3) of Example 1 above as a template. One hundred nanograms of the cDNA was used as a template, and the primers as shown by SEQ ID NO: 17 ~~SEQ ID NO: 13~~ and as shown by SEQ ID NO: 18 ~~SEQ ID NO: 14~~ were used. As the enzyme used for reaction, ExTaq (Takara Shuzo) was used. The reaction was carried out for 1 cycle at 94°C for 3 minutes; thereafter, 20 cycles at 94°C for 1 minute, 55°C for 1 minute, and 72°C for 2 minutes; and further at 72°C for 5 minutes. The resulting murine CXCR4 gene fragment was digested with NotI and XhoI (Takara Shuzo), and the digested fragment was incorporated into a NotI/XboI site of pCAGGStkNeo. The plasmid obtained in the manner described above was named pCANmPBSFR.--